



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Zheng J. Li, et al. :

APPLICATION NO.: 10/650,252 : Examiner: PESELEV, ELLI

FILING DATE: 08/27/03 : Group Art Unit: 1623

TITLE: CRYSTAL FORMS OF AZITHROMYCIN:  
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Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

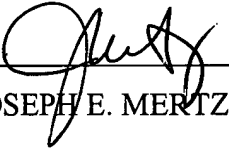
Sir:

I, Joseph E. Mertz, declare that:

1. I received my Bachelor of Science degree in Pharmacy in December 1994 from the College of Pharmacy and Health Sciences at Drake University in Des Moines, Iowa.
2. Since December 1994, I have been working at Pfizer, Inc. in Groton-CT on liquid formulations. I have also worked on determining the physical and chemical properties of new molecular entities (NME's) as it pertains to oral liquid and parenteral drug delivery.
3. Prior to May 8, 1998, I participated in the conception and reduction to practice of substantially pure Form F azithromycin claimed in the present application (see the X-RAY CRYSTALLOGRAPHY and Single Crystal X-Ray Crystallographic Analysis which are dated before May 8, 1998 and are attached herein as Exhibit 1). Exhibit 1 is redacted as to the dates of the documents which all occurred before May 8, 1998.
4. Exhibit 1 describes the crystal structure of a crystalline azithromycin compound having an azithromycin:water:ethanol ratio of about 1:1:0.5. I believe that the crystalline azithromycin is substantially pure Form F azithromycin. Such substantially pure Form F azithromycin was made and characterized prior to May 8, 1998.

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5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

  
JOSEPH E. MERTZ

07 Jul 2005  
DATE



EXHIBIT 1

**X-RAY CRYSTALLOGRAPHY**

JON BORDNER

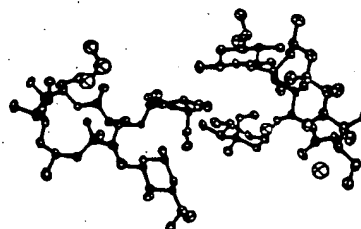
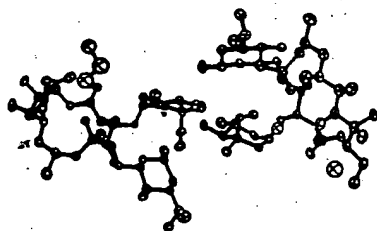
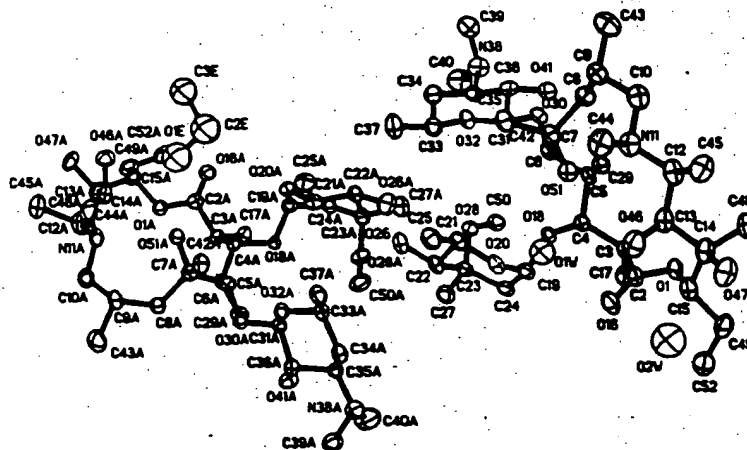
DEBRA DECOSTA

**PFIZER**  
**CENTRAL RESEARCH**  
**GROTON, CT 06340**  
**203-441-4510**

**PFIZER ID NUMBER:**  
**CP62,993-3 IN**  
**APRICOT OIL**

**X-RAY CODE:**  
**F112**

**INVESTIGATOR(S):**  
**MERTZ**





### A. Crystal Parameters

|  |   |
|--|---|
| formula                                    | $C_{38}H_{72}N_2O_{12} \cdot 2H_2O +$<br>$C_{38}H_{72}N_2O_{12} \cdot C_2H_5OH (1580.4)$  |
| crystallization medium                     | apricot oil and ethanol   |
| crystal size, mm                           | 0.14 X 0.20 X 0.24  |
| cell dimensions                            | $a = 16.281(2) \text{ \AA}$<br>$b = 16.293(1) \text{ \AA}$<br>$c = 18.490(3) \text{ \AA}$<br>$\alpha = 90.0^\circ$<br>$\beta = 109.33(1)^\circ$<br>$\gamma = 90.0^\circ$<br>$V = 4628(1) \text{ \AA}^3$ |
| space group                                | $P2_1$  |
| molecules/unit cell                        | 2   |
| density calcd, g/cm <sup>3</sup>           | 1.134   |
| linear absorption factor, mm <sup>-1</sup> | 0.692   |

### B. Refinement Parameters

|   |       |
|---|-------|
| number of reflections                             | 4975  |
| nonzero reflections ( $I > 3.0\sigma$ )           | 4350  |
| R-index <sup>a</sup>                              | 6.88% |
| GOF <sup>b</sup>                                  | 1.11  |
| secondary extinction factor <sup>c</sup> , $\chi$ | NONE  |

<sup>a</sup>  $R\text{-index} = \sum |F_o| - |F_c| / \sum |F_o|$

<sup>b</sup>  $GOF = [\sum w(F_o^2 - F_c^2)^2 / (m - s)]^{1/2}$

where  $w = [\sigma^2(F) + |g|F^2]^{-1}$   $g = .0073$

<sup>c</sup>  $F^* = F[1 + 0.002\chi F^2 / \sin(2\theta)]^{-1/4}$